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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/711,782	11/13/2000	Rex M. Bitner	16026-9264	7178

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EXAMINER
RILEY, JEZIA

ART UNIT	PAPER NUMBER
1637	10

DATE MAILED: 07/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/711,782	BITNER ET AL.	
	Examiner	Art Unit	
	Jezia Riley	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-51 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-51 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse in Paper No. 9 is acknowledged. The traversal is on the ground(s) that prior art search would require the search for all the species for R1, R2, and R3. This is not found persuasive because if a prior art search was done for all the species, it will encompassed an incredible amount of species. Therefore if all the species were searched together it will impose a serious burden on the examiner to look at each of them for enablement issues and art rejections.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

3. Claims 1-5, 7-36, are rejected under 35 U.S.C. 102(e) as being anticipated by Smith et al. (US 6,270,970 B1).

The reference relates generally to materials and methods for isolating nucleic acids, such as plasmid DNA, chromosomal DNA, total RNA, mRNA, viral DNA, viral RNA, or RNA/DNA hybrids from contaminants, such as proteins, lipids, cellular debris, or other nucleic acids. It relates, particularly, to solid phases, including magnetic or non-magnetic matrices and chromatographic stationary phases, which bind to a target nucleic acid under one set of solution conditions and release the target nucleic acid under another set of solution conditions. More particularly, this invention relates to mixed-bed solid phases comprising at least two different solid phases, wherein each solid phase in the mixture binds to and releases a target nucleic acid under different conditions.

The mixed-bed solid phase comprises a first solid phase and a second solid phase, wherein: the first solid phase has a capacity to bind to the target nucleic acid when combined with the mixture in the presence of a first solution, and a capacity to release the target nucleic acid bound thereto in the presence of a second solution; the second solid phase has a capacity to bind to the target nucleic acid when combined with the mixture in the presence of the second solution, and a capacity to release the target nucleic acid bound thereto in the presence of the first solution; and the first solid phase and the second solid phase each have a capacity to release the target nucleic acid bound thereto in the presence of an elution buffer. In another aspect, a mixed-bed solid phase for isolating a target nucleic acid from a mixture comprises the target nucleic acid

and at least one contaminant, the mixed-bed solid phase comprising first silica magnetic particles and second silica magnetic particles, wherein: (a) the first silica magnetic particles have a capacity to bind to the target nucleic acid when combined with the mixture in the presence of a first solution, and a capacity to release the target nucleic acid bound thereto in the presence of a second solution; (b) the second silica magnetic particles have a capacity to bind to the target nucleic acid when combined with the mixture in the presence of the second solution, and a capacity to release the target nucleic acid bound thereto in the presence of the first solution; and (c) the first silica magnetic particles and the second silica magnetic particles all have the capacity to release the target nucleic acid bound thereto in the presence of an elution buffer.

The first solid phase and second solid phase components of the mixed-bed solid phase of the present invention each have a capacity to bind to and release the target nucleic acid under different solution conditions. The first solid phase has the capacity to bind to the target nucleic acid in the presence of a first solution and to release the target nucleic acid in the presence of a second solution, while the second solid phase has the capacity to bind the target nucleic acid in the presence of the second solution and to release the target nucleic acid in the presence of the first solution. Thus, when the mixed-bed solid phase is combined with a mixture of the target nucleic acid and at least one contaminant in the presence of the first solution, the target nucleic acid binds to the first solid phase. When the mixed-bed solid phase is then separated from the first solution and combined with the second solution, the target nucleic acid is released from the first solid phase and binds to the second solid phase. The mixed-bed solid phase is

then separated from the second solution and combined with an elution buffer, wherein the target nucleic acid is released into the elution buffer. The mixed-bed solid phase is preferably combined with the first solution and separated therefrom, and/or combined with the second solution and separated therefrom at least one additional time before being combined with the elution buffer.

The first solid phase and the second solid phase can be made of silica. When the solid phase support material is silica, it is preferably in the form of silica gel, siliceous oxide, solid silica such as glass or diatomaceous earth, or a mixture of two or more of the above. At least one of the solid phases in the mixed-bed solid phase preferably comprises a silica gel particle. Silica materials, such as silica gel particles, can bind target nucleic acids in the presence of chaotropic agents. Chaotropic ions include guanidinium, iodide, perchlorate, and trichloroacetate. Chaotropic agents include guanidine hydrochloride, guanidine thiocyanate (which is sometimes referred to as guanidine isothiocyanate), sodium iodide, sodium perchlorate, and sodium trichloroacetate. Either the first solution or the second solution preferably contains at least 100 mM, more preferably at least 250 mM, and even more preferably at least 500 mM concentration of a chaotropic agent. The silica magnetic particles, wherein the diethylamino (DEA) anion exchange residue is covalently attached to the first silica magnetic particle through a propyl dimethoxy silane ligand.

4. Claims 1-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Smith et al. (US 6,310,199).

(US 6,310,199) discloses pH dependent ion exchange matrices, with methods for making such matrices, and methods for using such matrices to isolate a target nucleic acid, such as plasmid DNA, chromosomal DNA, or RNA from contaminants, including proteins, lipids, cellular debris, or other nucleic acids. Each pH dependent ion exchange matrix comprises at least two different ion exchange functional groups, one of which is capable of acting as an anion exchanger at a first pH, and the other of which is capable of acting as a cation exchanger at a second, higher pH. The matrix has an overall neutral charge in a pH range between the first and second pH. The pH dependent ion exchange matrices of the present invention are designed to bind to the target nucleic acid at a pH wherein the overall charge of the matrix is positive, and to release the target nucleic acid as the pH of the surrounding solution is increased. The target nucleic acid can be released from the pH dependent matrix in little or no salt and at about a neutral pH. The matrices and methods of this invention enable one to isolate a target nucleic acid in very few steps, without the use of hazardous chemicals. When the solid phase is silica based, each ion exchange ligand is preferably covalently attached to the solid phase through a silane group, as shown in formula (II). And example 3 shows the silane compound being identical to the instant invention. The anion exchange moiety and cation exchange moiety of the present matrix vary in charge depending upon solution conditions. In the presence of a solution having a first pH, the basic moiety (i.e., the amine) is positively charged and the matrix is capable of exchanging with the target nucleic acid. In the presence of a solution having a second pH which is higher than the first pH, the acidic moiety has a negative charge and the basic moiety has a neutral

charge. The matrix is designed to adsorb the target nucleic acid at the first pH and to desorb the target nucleic acid at a pH which is at least about the second pH. pH conditions necessary to ensure adsorption and desorption of the target nucleic acid to the matrix of the present invention depend upon the salt conditions of the adsorption and desorption solutions, and upon the specific composition and density of the plurality of ligands attached to the solid phase. Specifically, the first pH, at which desorption takes place, is preferably between pH 6 and 8 when the ionic strength of the solution is preferably no higher than about 1 M salt, more preferably no higher than about 500 mM salt, and most preferably no higher than about 50 mM salt. Nanopure water was used for washing step (see example 11).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (US 6,270,970 B1) or Smith et al. (US 6,310,199) in view of Smith (6,027,945).

Smith et al. discloses the invention as discussed above. However, no kit has been described.

Smith 6,027, 945 discloses kit for isolating a biological target material from a medium containing the same, the kit comprising an aliquot of siliceous-oxide coated magnetic particles suspended in an aqueous solution in a first container, wherein the particles have the capacity to reversibly bind at least 2 micrograms of the biological target material per milligram of particle. Optionally, the kit may include other components needed to isolate a biological target material from a medium containing the same.

Therefore it would have been obvious at the tie the invention was made to prepare kit for the method of (US 6,310,199) because it saves money and resources by reducing waste reagents since each of these reagents is needed in only small amounts

when beginning a series of experiments, thus reducing the accumulation of unused chemicals.

7. The references lined through in the PTO-1449s were not considered because either there was no publication date, duplicate, not available to the examiner, or not in the parent cases.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 703-305-6855. The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Patent Analyst Monica Graves whose telephone is 703-305-3002 or to the Technical Center receptionist whose telephone number is 703-308-0196.

JEZIA RILEY
PRIMARY EXAMINER

July 3, 2002